Remarks

Claims 89-182 are pending in the subject application. In response to a restriction requirement, claims 121-141, 150-152, and 163-182 were elected for examination on March 11, 2002. Certain of the claims have been amended for the purpose of expediting the patent application process in a manner consistent with the Patent and Trademark Office Patent Business Goals (PBG), 65 Fed. Reg. 54603 (September 8, 2000) and to advance prosecution and facilitate the business interests of Applicant(s). Support for these new claims and the amendments to the pending claims can be found throughout the subject specification, including, for example, at page 8, about line 16. Favorable consideration of the claims now presented, in view of the remarks and amendments set forth herein, is earnestly solicited.

The Office Action of August 23, 2002 has objected to the drawings and required corrections. Submitted herewith are corrected drawings for this matter.

The Office Action has also objected to the application on the grounds that certain of the Figures contain sequences not provided in the sequence listing that was filed with the above-referenced application. Applicants have submitted a substitute sequence listing with this response and believe that this issue is now moot.

The Office Action of August 23, 2002 also objected to the disclosure regarding the identical nature of SEQ ID NOs:1 and 12. Applicants have attended to this issue by indicating that these sequences are identical and that SEQ ID NO:1 and SEQ ID NO:12 can be used interchangeably throughout the subject specification. Additionally, any references to browser-executable code have been removed from the specification. Accordingly, withdrawal of the objection is respectfully requested.

The Office Action has also objected to the specification at page 190, lines 19-21, on the grounds that the paragraph structure is confusing and/or correlation to Tables 5 or 6. Applicants have deleted this paragraph and request withdrawal of the objection.

Claims 121-141, 150-152, and 163-182 have been rejected under 35 U.S.C. § 112, first paragraph, because the specification, while enabling for a method of identifying a nucleotide (allele T, marker A30) in cases of sporadic prostate cancer, does not reasonably provide enablement for the

identification of other nucleotides at other PCTA-1 biallelic markers in familial or sporadic prostate cancer. The Office Action further argues that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The Office Action argues that the statistical and numerical information provided in Tables 5 and 6 fails to enable the claimed invention and that the data is statistically insignificant as relates to the identification of sporadic or familial cases of prostate cancer. Applicants disagree and respectfully traverse.

As set forth at pages 105-106 and 189-193 of the subject application, haplotype association analysis that combines the A2 marker with other markers disclosed in the specification does provide for statistically significant associations of the haplotypes with familial or sporadic prostate cancer. For example, as set forth at pages 105-106, a three-marker haplotype including markers A2, A30, and A41 (ATT alleles respectively) was shown to be significantly associated with familial prostate cancer (Table 8, the "ATT" haplotype has a p-value of 2.5×10^{-7} for the familial early onset prostate cancer (see Example 5)). A two-marker haplotype including markers A2 and A57 (99-1605/112) (TA alleles, respectively) was shown to be significantly associated with sporadic prostate cancer. As shown in Table 8, the "TA" haplotype present a p-value of 3.4×10^{-5} for the sporadic informative prostate cancer (see Example 5). A second two-marker haplotype including markers A2 and A55 (5-2/178) (TT alleles, respectively) was shown to be significantly associated with prostate cancer, preferably with a sporadic prostate cancer. As shown in Table 8, the "TT" haplotype present a p-value of 1×10^{-5} for the sporadic informative prostate cancer (see Example 5). Permutation tests clearly validated the statistical significance of the association between these haplotypes and the prostate cancer (see Example 5).

As set forth at pages 189-193, combination of the A2 marker (allele A) with A30 (allele T) and A41 (allele T) provides for a statistically significant association of the haplotype with familial cases of prostate cancer. The combination of A2 with additional biallelic markers, such as A55 and/or A57 also provides for statistically significant associations with sporadic cases of prostate cancer. In view of these teachings of the specification, it is respectfully submitted that the invention is properly enabled and that undue experimentation and further direction is not required in view of the teachings of the specification. Withdrawal of the rejection is respectfully requested.

Even assuming that the enablement rejection of record is properly asserted, Applicants respectfully submit that the arguments advanced in support of this enablement rejection are not applicable to a number of the claims (claims 131-141) set forth in this application and that the rejection, as applied to these claims, is improper. For example, these claims are drawn to methods of genotyping comprising determining the identity of a nucleotide at a PCTA-1 related biallelic marker, or the complement thereof, in a biological sample; estimating the frequency of an allele of a PCTA-1-related biallelic marker in a population; detecting the association between a genotype and a trait; or estimating the frequency of a haplotype for a set of biallelic markers in a population. Applicants respectfully submit that one skilled in the art would be able to practice this aspect of the claimed invention without undue experimentation and that the specification enables the invention, as claimed. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

Claims 121-141, 150-152, and 163-182 have been rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not describe in the specification in such a way as to convey to one skilled in the art that the inventors were in possession of the claimed invention at the time the application was filed. Specifically, the Office Action argues that the specification fails to provide adequate written description of the claimed invention in that the claims are directed to gene sequences, mutated fragment sequences, allelic variants, splice variants, and so forth that have no written description in the application as filed. Applicants respectfully submit that this rejection is moot in view of the amendments made to the claims and the arguments presented in the traversal of the rejections set forth under 35 U.S.C. § 112, second paragraph.

Claims 121-141, 150-152, and 163-182 have been rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter regarded as the invention.

Claims 121, 140, 151, 152, 167-172, 177, and 178 have been indicated as indefinite in the recitation of "the complement". The Office Action indicates that the term can be interpreted as a sequence that is the same length and be the full and exact complement of the recited SEQ ID NO. Alternative interpretations are also given in the Office Action. Applicants respectfully submit that the term is fully understandable in the context of the claimed invention and that one skilled in the art would recognize that the phrase "complement thereof" related to the nucleotides identified as the

biallelic markers of the elected sequence. However, Applicants have amended the claims to more distinctly identify that such is the case and respectfully request withdrawal of the rejection.

Claims 121, 131, 132, 133, 150, 151, 152, 167, 168, 169, 170, 171, 172, 177, and 178, and the claims dependent therefrom, have been rejected as indefinite in the recitation of "PCTA-1-related biallelic marker". The Office Action argues that some degree of relatedness is implied by such a recitation. Applicants respectfully submit that the acceptability of the claim language depends on whether one of ordinary skill in the art would understand what is claimed, in light of the specification. As set forth in the specification at page 11, lines 22-25, the term "PCTA-1-related biallelic marker" relates to a set of biallelic markers in linkage disequilibrium with the PCTA-1 gene. Accordingly, it is respectfully submitted that the claims would not be vague or indefinite to one skilled in the art, and withdrawal of the rejection is respectfully requested.

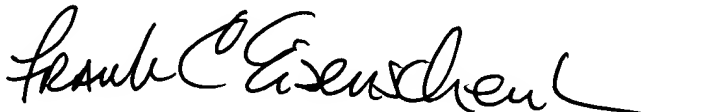
Claim 150 has been rejected as being indefinite the lack of a recitation of a final process step that relates back to the preamble of the claim. Applicants submit that this rejection is moot in view of the amendments made to the claim.

Claims 140 and 141 have been rejected as lacking antecedent basis in the claims from which each of the claims depend. With respect to the rejection as applied to claims 140 and 141, Applicants respectfully submit that the term "control population" can be found in step b) of claim 132. This rejection, as applied to "case control population" is also moot in view of the amendment made to the claims.

In view of the foregoing remarks and the amendments to the claims, the applicant believes that the pending claims are now in condition for allowance, and such action is respectfully requested. The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§ 1.16 or 1.17 as required by this paper to Deposit Account 19-0065.

Applicants also invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephone interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,



Frank C. Eisenschenk, Ph.D.
Patent Attorney
Registration No. 45,332
Phone: 352-375-8100
Fax No.: 352-372-5800
Address: Saliwanchik Lloyd & Saliwanchik
A Professional Association
2421 NW 41st Street, Suite A-1
Gainesville, FL 32606-6669

FCE/jaj

Attachments: Marked-Up Version of Amended Specification Paragraphs
Marked-Up Version of Amended Claims
Substitute Figures (Sheets 1-11)
Submission of Substitute Sequence List
Amendment regarding Sequence List
Paper Version of Substitute Sequence List
Electronic Version (CRF) of Substitute Sequence List
Petition for 3-Month Extension of Time (in duplicate)

MARKED-UP VERSION OF AMENDED SPECIFICATION PARAGRAPH

Please replace the paragraph beginning at page 169, line 29 with the following paragraph:

Figure 6 is a flow diagram illustrating one embodiment of an identifier process 300 for detecting the presence of a feature in a sequence. The process 300 begins at a start state 302 and then moves to a state 304 wherein a first sequence that is to be checked for features is stored to a memory 115 in the computer system 100. The process 300 then moves to a state 306 wherein a database of sequence features is opened. Such a database would include a list of each feature's attributes along with the name of the feature. For example, a feature name could be "Initiation Codon" and the attribute would be "ATG". Another example would be the feature name "TAATAA Box" and the feature attribute would be "TAATAA". An example of such a database is produced by the University of Wisconsin Genetics Computer Group (Worldwide Web address: ~~www.~~gcg.com).

MARKED-UP VERSION OF AMENDED CLAIMS

121. (Amended) A method of genotyping comprising determining the identity of a nucleotide at a PCTA-1-related biallelic marker, or the complement of said nucleotide~~thereof~~, in a biological sample.

141. (Thrice Amended) The method according to claim 132, wherein said ~~case~~-control population is a random population.

150. (Amended) A method of determining whether an individual is at risk of developing prostate cancer, comprising:

a) genotyping at least one PCTA-1-related biallelic marker according to the method of claim 123; and

b) correlating the result of step a) with one or more biallelic marker that is associated with a risk of developing prostate cancer.

151. (Thrice Amended) The method according to claim 121, wherein said PCTA-1-related biallelic marker is selected from the group consisting of biallelic markers of SEQ ID No:1 located at positions 278, 402, 472, 2955, 12167, 12536, 17593, 17606, 22079, 28964, 29003, 31077, 31766, 34791, 45751, 49847, 49855, 49886, 49900, 49906, 49921, 49939, 50256, 54955, 64239, 65436, 65496, 66967, 66987, 67092, 67129, 67229, 67433, 67723, 67834, 67955, 68213, 68263, 68375, 68477, 68525, 68594, 68610, 70566, 70728, 80038, 80118, 80170, 80183, 80435, 82090, 82165, 82169, 82218, 82234, 82268, 82393, 83587, 83643, 83644, 83808, 83881, 83884, 83909, 83937, 83947, 83982, 83988, 84047, 84092, 84145, 85202, 86259, 86323, 87713, 87735, 87787, 87806, 87860, 87902, 87980, 88012, 88215, 88283, 88297, 88442, 88471, 88480, 89394, 89464, 89471, 89658, 92760, 93023, 93055, 93247, 93319, 93323, 93388, 93393, 93418, 93515, 93726, 93903, 94170, 94218, 94269, 94290, 94422, 94432, 94720, 94989, 95261, 95340, 95497, 95770, 95819, 96145, 96181, 96350, 96951, 97144, 97276, 102267, 105937 and any complements of said biallelic marker ~~thereof~~.

152. (Fourth Amendment) The method according to claim 150, wherein said PCTA-1-related biallelic marker is at least one PCTA-1-related biallelic marker located at position 402, 67092, 68525, 82234, or 82393 of SEQ ID NO. 1, and any complement of said biallelic marker ~~thereof~~.

167. (Twice Amended) The method according to claim 131, wherein said PCTA-1-related biallelic marker is selected from the group consisting of biallelic markers of SEQ ID No:1 located at positions 278, 402, 472, 2955, 12167, 12536, 17593, 17606, 22079, 28964, 29003, 31077, 31766, 34791, 45751, 49847, 49855, 49886, 49900, 49906, 49921, 49939, 50256, 54955, 64239, 65436, 65496, 66967, 66987, 67092, 67129, 67229, 67433, 67723, 67834, 67955, 68213, 68263, 68375, 68477, 68525, 68594, 68610, 70566, 70728, 80038, 80118, 80170, 80183, 80435, 82090, 82165, 82169, 82218, 82234, 82268, 82393, 83587, 83643, 83644, 83808, 83881, 83884, 83909, 83937, 83947, 83982, 83988, 84047, 84092, 84145, 85202, 86259, 86323, 87713, 87735, 87787, 87806, 87860, 87902, 87980, 88012, 88215, 88283, 88297, 88442, 88471, 88480, 89394, 89464, 89471, 89658, 92760, 93023, 93055, 93247, 93319, 93323, 93388, 93393, 93418, 93515, 93726, 93903, 94170, 94218, 94269, 94290, 94422, 94432, 94720, 94989, 95261, 95340, 95497, 95770, 95819, 96145, 96181, 96350, 96951, 97144, 97276, 102267, 105937 and any complements of said biallelic marker ~~thereof~~.

168. (Twice Amended) The method according to claim 132, ~~,~~ wherein said PCTA-1-related biallelic marker is selected from the group consisting of biallelic markers of SEQ ID No:1 located at positions 278, 402, 472, 2955, 12167, 12536, 17593, 17606, 22079, 28964, 29003, 31077, 31766, 34791, 45751, 49847, 49855, 49886, 49900, 49906, 49921, 49939, 50256, 54955, 64239, 65436, 65496, 66967, 66987, 67092, 67129, 67229, 67433, 67723, 67834, 67955, 68213, 68263, 68375, 68477, 68525, 68594, 68610, 70566, 70728, 80038, 80118, 80170, 80183, 80435, 82090, 82165, 82169, 82218, 82234, 82268, 82393, 83587, 83643, 83644, 83808, 83881, 83884, 83909, 83937, 83947, 83982, 83988, 84047, 84092, 84145, 85202, 86259, 86323, 87713, 87735, 87787, 87806, 87860, 87902, 87980, 88012, 88215, 88283, 88297, 88442, 88471, 88480, 89394, 89464, 89471, 89658, 92760, 93023, 93055, 93247, 93319, 93323, 93388, 93393, 93418, 93515, 93726, 93903, 94170, 94218, 94269, 94290, 94422, 94432, 94720, 94989, 95261, 95340, 95497, 95770, 95819,

96145, 96181, 96350, 96951, 97144, 97276, 102267, 105937 and any complements of said biallelic markerthereof.

169. (Twice Amended) The method according to claim 133, wherein said PCTA-1-related biallelic marker is selected from the group consisting of biallelic markers of SEQ ID No:1 located at positions 278, 402, 472, 2955, 12167, 12536, 17593, 17606, 22079, 28964, 29003, 31077, 31766, 34791, 45751, 49847, 49855, 49886, 49900, 49906, 49921, 49939, 50256, 54955, 64239, 65436, 65496, 66967, 66987, 67092, 67129, 67229, 67433, 67723, 67834, 67955, 68213, 68263, 68375, 68477, 68525, 68594, 68610, 70566, 70728, 80038, 80118, 80170, 80183, 80435, 82090, 82165, 82169, 82218, 82234, 82268, 82393, 83587, 83643, 83644, 83808, 83881, 83884, 83909, 83937, 83947, 83982, 83988, 84047, 84092, 84145, 85202, 86259, 86323, 87713, 87735, 87787, 87806, 87860, 87902, 87980, 88012, 88215, 88283, 88297, 88442, 88471, 88480, 89394, 89464, 89471, 89658, 92760, 93023, 93055, 93247, 93319, 93323, 93388, 93393, 93418, 93515, 93726, 93903, 94170, 94218, 94269, 94290, 94422, 94432, 94720, 94989, 95261, 95340, 95497, 95770, 95819, 96145, 96181, 96350, 96951, 97144, 97276, 102267, 105937, and any complements of said biallelic markerthereof.

170. (Twice Amended) The method according to claim 135, wherein said PCTA-1-related biallelic marker is selected from the group consisting of biallelic markers of SEQ ID No:1 located at positions 278, 402, 472, 2955, 12167, 12536, 17593, 17606, 22079, 28964, 29003, 31077, 31766, 34791, 45751, 49847, 49855, 49886, 49900, 49906, 49921, 49939, 50256, 54955, 64239, 65436, 65496, 66967, 66987, 67092, 67129, 67229, 67433, 67723, 67834, 67955, 68213, 68263, 68375, 68477, 68525, 68594, 68610, 70566, 70728, 80038, 80118, 80170, 80183, 80435, 82090, 82165, 82169, 82218, 82234, 82268, 82393, 83587, 83643, 83644, 83808, 83881, 83884, 83909, 83937, 83947, 83982, 83988, 84047, 84092, 84145, 85202, 86259, 86323, 87713, 87735, 87787, 87806, 87860, 87902, 87980, 88012, 88215, 88283, 88297, 88442, 88471, 88480, 89394, 89464, 89471, 89658, 92760, 93023, 93055, 93247, 93319, 93323, 93388, 93393, 93418, 93515, 93726, 93903, 94170, 94218, 94269, 94290, 94422, 94432, 94720, 94989, 95261, 95340, 95497, 95770, 95819, 96145, 96181, 96350, 96951, 97144, 97276, 102267, 105937 and any complements of said biallelic marker thereof.

171. (Twice Amended) The method according to claim 150, wherein said PCTA-1-related biallelic marker is selected from the group consisting of biallelic markers of SEQ ID No:1 located at positions 278, 402, 472, 2955, 12167, 12536, 17593, 17606, 22079, 28964, 29003, 31077, 31766, 34791, 45751, 49847, 49855, 49886, 49900, 49906, 49921, 49939, 50256, 54955, 64239, 65436, 65496, 66967, 66987, 67092, 67129, 67229, 67433, 67723, 67834, 67955, 68213, 68263, 68375, 68477, 68525, 68594, 68610, 70566, 70728, 80038, 80118, 80170, 80183, 80435, 82090, 82165, 82169, 82218, 82234, 82268, 82393, 83587, 83643, 83644, 83808, 83881, 83884, 83909, 83937, 83947, 83982, 83988, 84047, 84092, 84145, 85202, 86259, 86323, 87713, 87735, 87787, 87806, 87860, 87902, 87980, 88012, 88215, 88283, 88297, 88442, 88471, 88480, 89394, 89464, 89471, 89658, 92760, 93023, 93055, 93247, 93319, 93323, 93388, 93393, 93418, 93515, 93726, 93903, 94170, 94218, 94269, 94290, 94422, 94432, 94720, 94989, 95261, 95340, 95497, 95770, 95819, 96145, 96181, 96350, 96951, 97144, 97276, 102267, 105937 and any complements of said biallelic marker ~~thereof~~.

177. (Twice Amended) The method according to claim 133, wherein said PCTA-1-related biallelic marker is at least one PCTA-1-related biallelic marker located at position 402, 67092, 68525, 82234, or 82393 of SEQ ID NO. 1, and any complement ~~thereof~~ of said biallelic marker.

178. (Amended) The method according to claim 177, wherein said PCTA-1-related biallelic marker is a combination of more than one PCTA-1-related biallelic marker or any complement of said biallelic marker~~thereof~~.